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29 April 1959

52-D COMPARISON OF EFFECTS OF C-9 DISSOLVED IN OIL WITH THOSE OF C-9 DISSOLVED IN ALCOHOL.

PURPOSE: To determine if C-9 dissolved in oil is as active as C-9 dissolved in alcohol and administered dispersed in watery solution.

METHODS:

Subjects: Five nontolerant former morphine addicts, all male, who were serving sentences for violation of the federal narcotic laws were used in these experiments. All were physically healthy, presented no evidence of the major psychoses, and all had experienced the effects of marihuana in a free environment.

Drugs: All drugs were given at 8 a.m. with the patients fasting. C-9 was available as a solution containing 10 mg/ml in vegetable oil in perles. The perles were opened, the doses measured and diluted with 8 cc of vegetable oil ("Mazola"). The glass was rinsed with 2 additional portions of 4 cc of oil. Vegetable oil containing no drug was used as a placebo. C-9 was also available as a solution of 1 mg/ml in 95 per cent ethanol. The dose was measured and diluted with 8 cc of distilled water, forming a milky suspension. The glass was rinsed with two portions of water.

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Design: The patients received at weekly intervals, in a randomized, balanced order, the following drugs: 1.0 and 1.5 mg per 70 kg of C-9 in oil; 1.0 and 1.5 mg/70 kg of C-9 in alcohol; and a placebo. The patients were unaware of the identity of the drugs ("single-blind" procedure).

Observations: The following observations were made at hourly intervals twice before and eight times after the drugs: pulse rate and blood pressure after ten minutes rest in bed, pulse rate and blood pressure after arising from bed and standing quietly for one minute, and rectal temperature. In addition, patients completed a questionnaire containing 67 items at hourly intervals, once before and eight times after the drug.

Analysis: In the cases of rectal temperature, resting and standing pulse rates, and resting and standing blood pressures, the values at each hour after the drug were subtracted from the average of the predrug observations. These values for change from control constituted time-action curves, so the areas under these curves were calculated and the usual statistical calculations made using the t-test for paired observations. Questions scored positively after the drugs were counted over the entire post-drug period, eliminating answers also scored positively prior to the drug.

RESULTS

The results are summarized in table 1. All doses of C-9 in both alcohol and oil consistently elevated resting and standing pulse rates, decreased the usual rise in resting blood pressure, and caused postural hypertension. Rectal temperature was not consistently affected. In general, C-9 dissolved in alcohol was consistently more effective than C-9 dissolved in oil, thought the differences did not reach statistical significance. There was no significant difference in onset and peak time of the changes in pulse rate and standing blood pressures. The usual subjective reports -- change in mood, mild perceptual distortion, dry mouth, dizziness and sleepiness -- were reported after both oily and alcoholic solutions.

Four of 5 patients fainted on standing after 1.5 mg of C-9 in alcohol, whereas only one of 5 fainted after 1.5 mg of C-9 in oil. One patient fainted after 1.0 mg in alcohol, and none after 1.0 mg in alcohol.

Conclusion: C-9 dissolved in oil is effective in inducing postural hypertension and marihuana-like subjective effects, but is probably less effective than C-9 in alcohol.

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Table 1.

Comparison of Effects of C-9 in Alcohol with Those in Oil.

MEASURE	DOSE AND VEHICLE				
	Placebo (Oil)	Oil (1.0 mg)	Alcohol (1.0 mg)	Oil (1.5 mg)	Alcohol (1.5 mg)
Resting Pulse Rate	+45.6 ± 19	+51.6 ± 16.5	+63.6 ± 18	+72.8 ± 10.3	94.3 ± 19.6
St iing Pulse Rate	-10.2 ± 30.9	+81.6 ± 36	+95.3 ± 45.6	+87.1 ± 25.8	+118.7 ± 46
Resting Blood Pressure	+64.8 ± 33.6	+15.0 ± 33	+31.9 ± 18	+34.3 ± 11.5	+22.7 ± 17.8
Standing Blood Pressure	+40.1 ± 14.8	+19.3 ± 35	-38.8 ± 34.1	-93.4 ± 23.2	-110.6 ± 39.5
Temperature	+ 1.9 ± 0.6	+ 2.4 ± 0.35	+ 1.4 ± 0.5	+ 0.9 ± 0.9	+ 1.04 ± 0.2
Number of Positive Responses on Questionnaire	1.6 ± 1.2	11.0 ± 4.2	11.0 ± 3.1	8.0 ± 3.1	18.2 ± 6.55

Figures are the means (5 subjects) of areas under the time-action curves for the various measures ("beat-hours," "mm-hours," etc., except in case of number of positive responses on the questionnaire). A positive sign indicates an increase in the measurement, a negative sign a decrease.